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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,149	12/23/2005	Matthias Vennemann	VOSS-0030	5535

7590 05/27/2009

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EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
05/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,149	VENNEMANN ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 21-23* is/are pending in the application.

4a) Of the above claim(s) *22 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18, 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-23 are pending.

Applicants have elected group I , claims 1-18 and 21

Group I, claim(s) 1-18 and 21, drawn to compounds and pharmaceutical compositions of formula I wherein R2 and R3 do not form a ring, none of the R's form a ring (i.e. it is a tricyclic ring) and R7 is a phenyl or naphthyl (substituted or unsubstituted).

Applicants traversal regarding the restriction has been acknowledged but is not found to be convincing.

Applicants argue that patent Office has not established that it would pose an undue burden to examine the full scope. The examiner has made a lack of Unity.

This is incorrect as when the core was searched the examiner found many iterations.

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L1 HAS NO ANSWERS
L1                STR
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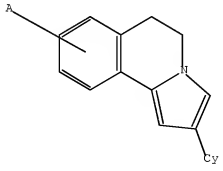


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Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 12:44:50 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    15707 TO ITERATE

 12.7% PROCESSED     2000 ITERATIONS                          4 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       306632 TO   321648.
 The projected iterations were about 321 thousand compounds.
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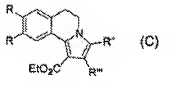
Bauser et al WO 03014117 discloses the compounds of the formula



R = H, OCH_3
R" = CH_3, C_6H_5
R''' = C_6H_5

on page 4. The reference recites Liebigs Ann. Chem 9, 1534 -1544 Meyer This reads on the applicants claimed compounds of formula I wherein R7 is a phenyl, R1 , R2 are alkoxy, r3 is a H, R4, R41 are H, R5 and R51 are also H, R6 , R61 is a carboxy, R 8 is a COOR9, R9 is H.

So the lack of unity has been maintained and has been made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10, 11 and 17 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for substitutents to be H, alkyl, alkoxycarbonylalkyl, cyano, , does not reasonably provide enablement for all the various substitutents nor for the hydrates and hydrates of the salts thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it.

2) The nature of the invention: The invention is a (highly) substituted compound for regulating fertility in mammals.

3) The state of the prior art: There is very little know in the regulation of fertility. Also synthesizing compounds is very unpredictable. The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the activity as a PDE inhibitors as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an

area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group. The method of making theses compounds with numerous functional groups is also very unpredictable as these groups may react with each other and would require an undue amount of experimentation to make these compounds.
As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

Regarding hydrates:- The claims are drawn to hydrates, yet the numerous examples presented all failed to produce a hydrate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that hydrates can be made, or limit the claims accordingly.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are examples to just a limited scope of compounds.

7) The existence of working examples: The instant specification does not have any working examples. On page 85 there is some data for antiproliferative activity.
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 103

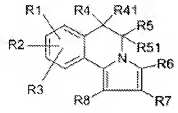
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10-14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over. WO 2003051877 Zang et al ,

Bauser et al WO 03014117 and WO 03014116.

Applicants claims are drawn to the compounds of the formula i

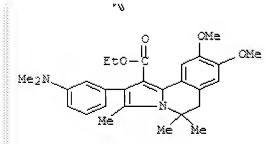


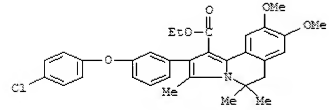
(I)

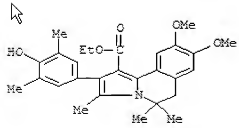
, R7 is a phenyl or naphthyl., and all

R4, R41, R5, R51, R6 an all be H.

Such as

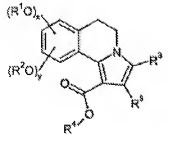






Scope & Content of Prior Art MPEP 2141.01

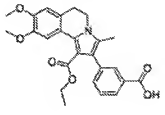
WO '877 teaches compounds of the formula



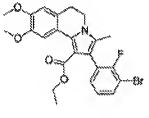
(I)

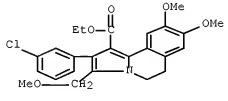
wherein

, R5 is a phenyl. R3 is an alkyl optionally substituted by halogens., r4 is also an alkyl , R1 and R2 are H or alkyls.

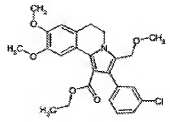


Specific examples are



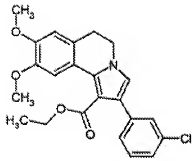


Bauser et al WO 03014117 and WO 03014116 teaches compounds which are given as



See claim 5 see examples 23, 24 on page 64.

See example 21 on page 62



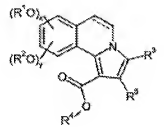
Difference between Prior Art and the claims MPEP 2141.02

The difference is only in the substitutents on the R5 phenyl ring.

These compounds also have the same PDE inhibition activity which in turn is drawn to inhibiting cellular proliferation (according to applicants own admission on page 2 paragraph 1 of the specifications.). These read on the generic compounds.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

One skill in the art would have found it obvious to make the compounds as the generic disclosure in the prior art is very large such as given below



(I)

wherein

x and y independently from each other denote zero or 1 and x+y is 1 or 2;

R^1 and R^2 independently from each other denote hydrogen, C_{1-4}-alkyl or CF_3, or R^1 and R^2 together form a C_{1-4}-alkylene bridge;

R^3 denotes hydrogen, formyl, (C_{1-4}-alkyl)-carbonyl, (C_{1-4}-alkoxy)-carbonyl, NO_2, NR^6R^7, C_{1-4}-alkyl-NR^6R^7, C_{1-4}-alkyl-OR^8, C_{1-4}-alkyl-$COOR^8$, C_{6-10}-aryl-C_{1-4}-alkyl wherein the aryl moiety is optionally substituted with 1 to 3 radicals selected from the group consisting of OH, C_{1-4}-alkyl, and C_{1-4}-alkoxy;

wherein

R^6 and R^7 independently from each other denote hydrogen, C_{1-4}-alkyl, C_{3-8}-cycloalkyl, or C_{6-10}-aryl-C_{1-4}-alkyl wherein the aryl moiety is optionally substituted with 1 to 3 radicals selected from the group consisting of OH, C_{1-4}-alkyl and C_{1-4}-alkoxy;

R^5 is

i) phenyl optionally having 1 to 3 further substituents selected from the group consisting of F, Cl, Br; C_{1-6}-alkyl; C_{1-6}-alkoxy; OH; NR^9R^{10} and $COOR^{11}$;

or

ii) naphthyl optionally containing one further OH group;

or

Thus modifying compounds by changing the H to an alkyl group or or an hydroxyl or halogen groups would be prima facie obvious as the prior art teaches them and also shows many species covering the various substituents at the different positions.

Compounds which have a close similarity in structure would be expected to have similar properties and hence motivating one to modify them to obtain new compounds.

H vs Me is not considered a patentable distinction absent evidence of superior, unexpected results. Note In re Wood 199 USPQ 137; In re Lohr 137 USPQ 548; In re Fauque 121 USPQ 425.

Rejections based on structural similarities is founded on the expectations that compounds similar in structure will have similar properties. Note MPEP 2144.09.

Double Patenting

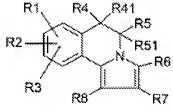
A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v.*

Eagle Mfg. Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim1, and 21 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 , and 17 of copending Application No. 10562137. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

1. (Currently amended) ~~Compounds~~ A compound of formula I



(I)

in which

The examiner has made a statutory DP because she has made a restriction and limited R7 to be a phenyl group in the instant application. The claims in the co-pending application has also the same elected group.

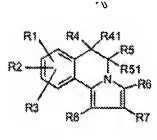
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim1-8,10-14 and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 11794497. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same core.

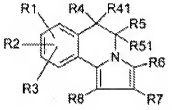


(I)

. The examiner has not made a statutory DP because she has made a restriction and limited R7 to be a phenyl group in the instant application. The claims in the co-pending application include the elected subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-8, 10-14 and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 10 of copending Application No.11794494. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to the same core.



(I)

. The examiner has not made a statutory DP because she has made a restriction and limited R7 to be a phenyl group in the instant application. The claims in the co-pending application include the elected subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 1-18 and 21 are rejected.

Claims 22, 23 are are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

May 21, 2009

/Rita J. Desai/

Primary Examiner, Art Unit 1625